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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	ARORA et al.	Customer No.:	26815
Serial No.:	10/611,386	Examiner:	Devesh Khare
Filing Date:	July 1, 2003	Group Art Unit:	1623
Title:	DERIVATIVES OF MONOSACCHARIDES AS CELL ADHESION INHIBITORS		

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Michelle Morgan

EV674777080US

IN THE BOARD OF APPEALS AND INTERFERENCES
OF THE UNITED STATES PATENT & TRADEMARK OFFICE

Applicant: ARORA *et al.*

Examiner: Devesh Khare

Application No.: 10/611,386

Group Art Unit: 1623

Filing Date: July 1, 2003

Divisional Application of Serial No. 09/276,368 filed March 25, 1999

For: **DERIVATIVES OF MONOSACCHARIDES AS CELL ADHESION INHIBITORS**

BRIEF ON APPEAL

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Commissioner:

1. Real Party in Interest

The real party in interest in this case is Ranbaxy Laboratories Limited, the Assignee of the present application, the assignment being recorded at Reel 01050/Frame 0867.

2. Related Appeals and Interferences

There are simultaneously pending appeals in the following cases related to this case:

Serial No. 10/610,719 filed July 1, 2003, Divisional Application of Serial No. 09/276,368 filed March 25, 1999, now U.S. Patent No. 6,590,085 issued July 8, 2003;

Serial No. 10/611,093 filed July 1, 2003, Divisional Application of Serial No. 09/276,368 filed March 25, 1999, now U.S. Patent No. 6,590,085 issued July 8, 2003;

Serial No. 10/611,091 filed July 1, 2003, Divisional Application of Serial No. 09/276,368 filed March 25, 1999, now U.S. Patent No. 6,590,085 issued July 8, 2003.

3. Status of Claims

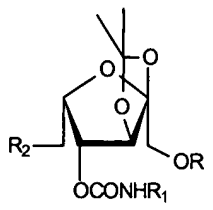
Claims 5 and 6 are pending in the application. A copy of the pending claims is provided in the Appendix. Claims 5 and 6 have been finally rejected in the application.

4. Status of Amendments

No amendment has been filed subsequent to the Final Office Action.

5. Summary of Invention

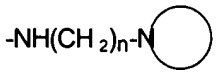
An aspect of the present invention is to provide processes for synthesizing a new class of compounds that exhibit significant activity as VLA_4 antagonists. It is a further aspect of this invention to provide processes for the preparation of novel carbohydrate-based water-soluble compounds that exhibit significant activity to be used as cell-adhesion antagonists. Further, pharmaceutically useful compositions containing compounds in this new class are provided. Methods of treating cell-adhesion and cell-adhesion mediated pathologies using the pharmaceutical compositions are also provided. In order to achieve the above-mentioned aspects, and in accordance with one aspect of the present invention, there is provided a process for the synthesis of monosaccharide derivatives and the derivatives themselves, having a structure of Formula I:



FORMULA I

or its pharmaceutically acceptable salts, esters, enantiomers, diastereomers, N-oxides, amides, wherein R is C_1 to C_{15} alkyl, alkene, alkyne (straight chain or branched), aryl, or alkylaryl and R_1 is methyl, phenyl o-, m- or p-chlorophenyl, tolyl, methoxyphenyl or

nitrophenyl and R_2 is H, pyrrolidinyl, piperidinyl, morpholinyl or hexamethyleneamino or a radical of the formula NHR_3, wherein R_3 is C_1 to C_{15} alkyl, alkene or alkyne (straight chain or branched) or a radical of Formula III



FORMULA III

wherein n is 2 to 5 and

is a five-, six- or seven-membered heterocyclic ring containing one or more heteroatoms.

6. Issues

Claims 5 and 6 are rejected under 35 U.S.C. §103(a).

7. Grouping of Claims

All the claims appealed herein stand or fall together.

8. Argument

Claims 5 and 6 are not Obvious Over Arora et al. (United States Patent No. 5,637,570) in view of Bouveng (Acta. Chem. Scand., 1961, 15, pp 96-100)

Claims 5 and 6 have been rejected as obvious over Arora et al. in view of Bouveng. Applicants respectfully traverse the rejection for the following reasons.

The Examiner's position is that processes disclosed in Arora et al. in combination with the disclosure of Bouveng, makes applicants' instant claims obvious. As an initial matter, it is clear that Arora et al. differs from the instant claims, in that the disclosure of Arora et al. is directed to compounds wherein the sugar is not substituted with a carbamate moiety.

Further, there is no teaching or suggestion in Arora et al. to employ processes to create a carbamate group at the 4-position of the compound of Formula I. The disclosure of Arora et al. shows that R_2 in the $-OR_2$ group can take the values of hydrogen, C_{10}-C_{15} alkyl, $-(CH_2)_{n3}$-N-[cyclic alkyl group optionally containing an oxygen atom] or $-(CH_2)_{n5}$-$N(CH_3)_2$, wherein n3 and n5 can be 2-6 and 2-4 respectively.

The Examiner asserts that "[i]t would have been obvious to person having ordinary skill in the art at the time the invention was made, to modify the process for conversion of the 4-hydroxy group to its corresponding nitrogen containing heterocyclic moiety of Arora in view of the teachings of Bouveng to a process of conversion of a free hydroxyl group to its corresponding carbamate by treating with an isocyanate reagent because Arora discloses that the said compounds exhibit greater potency for cancer treatment and provides ease of oral administration when the 4-OH is substituted with a nitrogen containing heterocyclic moiety." (pages 3-4, Final Action).

Applicants strongly and respectfully disagree with the quoted statement to the extent that the Examiner is suggesting that Arora et al. discloses applicants' claimed processes for making the particular compounds, suggests applicants' claimed processes for making the particular compounds, or contains any disclosure or suggestion of the usefulness of applicant's claimed processes for making the particular compounds.

The Examiner states that "one skilled in the art would have a reasonable expectation for success in combining the teachings of Arora et al. and Bouveng references to accomplish the compounds of 2,3-O-isopropylidene-α-L-xylo-2-hexulofuranosonic acid of Formula I (Arora et al.) wherein sugar is substituted with a carbamate group (Bouveng)."

In fact, Arora et al. contains no suggestion or motivation for modification of the compounds of Formula I at the 4-position of the structure whatsoever. The exact language of Arora et al. is actually the following: "It appears that L-hexoses coupled with substitution at the 1-position (preferably alkyl) and another substitution at 5- and/or 6-position (preferably o-heterocyclic alkyl, heterocyclic alkyl, N-heterocycle, N-heterocyclic alkyl, etc.) plays an important role for displaying significant activity..." (col. 2, lines 38-43; emphasis added). Thus, there is no mention at all of the 4-position, much less a suggestion to modify or substitute the Arora et al. compounds at the 4-position, and even further removed from any hint that the 4-position of Arora et al. compounds should or might be substituted with a carbamate.

To remedy this deficiency, the Examiner attempts to combine Arora et al. with Bouveng. This latter publication appears to disclose the investigation of the distribution of O-acetyl groups in glucuronoxylan from birch wood using phenylcarbamoyl groups as protective substituents (see Abstract).

It does not appear that the cited reference is at all relevant to the obviousness (*vel non*) of the claimed processes. There does not appear to be any disclosure or suggestion of the processes to make 2,3-O-isopropylidene-α-L-xylo-2-hexulofuranose compounds. The teaching of the reference, namely that a 4-hydroxyl group can be transformed to a phenylcarbamoyl group in a carbohydrate of no relevance to applicants' claimed compounds, does not constitute a *prima facie* case of obviousness in the present case.

Furthermore, there appears to be no pharmaceutical application to the Bouveng reference in the slightest. It is inconceivable that one of ordinary skill in the art, considering processes to make the compounds disclosed in Arora et al., would look to the

disclosure of Bouveng to arrive at a process to create a 4-carbamate hexulofuranose with any expectation whatsoever that such a compound could have any utility as a pharmaceutical agent.

There is no suggestion or motivation contained in the Bouveng reference to arrive at applicants' claimed processes. Again, absent such suggestion or motivation, the Examiner's position that it would have been obvious to combine Arora et al. with Bouveng is pure and impermissible hindsight. Applicants respectfully request that the rejection be reconsidered and withdrawn.

Conclusion

In light of the foregoing, applicants submit that the claims are not obvious under 35 U.S.C. §103(a). Therefore, the rejection of claims 5 and 6 should be withdrawn and the claims should be allowed.

Respectfully submitted,
ARORA *et al.*

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Date: June 8, 2005

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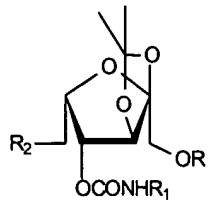
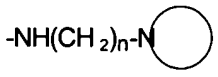
APPENDIX

5. A process for preparing compounds of Formula I:



FORMULA I

and its pharmaceutically acceptable salts, esters, enantiomers, diastereomers, N-oxides, amides, wherein R is C_1 to C_{15} alkyl, alkene, alkyne (straight chain or branched), aryl, substituted aryl or alkylaryl and R_1 is methyl, phenyl o-, m- or p-chlorophenyl, tolyl, methoxyphenyl or nitrophenyl and R_2 is H, pyrrolidinyl, piperidinyl, morpholinyl or hexamethyleneimino or a radical of the formula NHR_3, wherein R_3 is C_1 to C_{15} alkyl, alkene or alkyne (straight chain or branched) or a radical of Formula III:

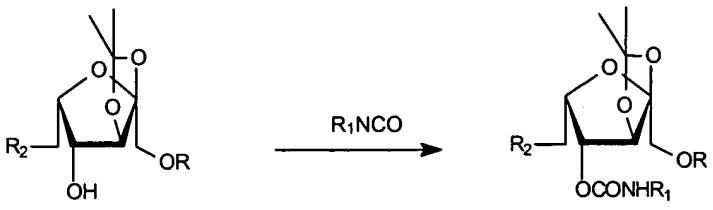


FORMULA III

wherein n is 2 to 5 and

is a five-, six- or seven-membered heterocyclic ring containing one or more heteroatoms,

the process comprising treating the compound of Formula II with an isocyanate in a solvent as follows:



FORMULA II **FORMULA I**

6. (Original) A process according to claim 5, wherein

is pyrrolidinyl, piperidinyl, morpholinyl or hexamethyleneimino.